Listing of Claims

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1-108. (Cancelled)

109. (New) A molecular biosensor, the biosensor having two nucleic acid constructs, the nucleic acid constructs comprising:

$$R^{1}-R^{2}-R^{3}-R^{4}$$
; and $R^{5}-R^{6}-R^{7}-R^{8}$:

wherein:

R¹ is an epitope binding agent that binds to a first epitope on a target molecule;

 R^2 is a flexible linker attaching R^1 to R^3 ;

R³ and R⁷ are a pair of complementary nucleotide sequences having a free energy for association from about 5.5 kcal/mole to about 8.0 kcal/mole at a temperature from about 21° C to about 40° C and at a salt concentration from about 1 mM to about 100 mM; R⁴ and R⁸ together comprise a detection means such that when R³ and R⁷ associate a detectable signal is produced;

 R^5 is an epitope binding agent that binds to a second epitope on the target molecule; and R^6 is a flexible linker attaching R^5 to R^7 .

- 110. (New) The molecular biosensor of claim 109, wherein the target molecule is selected from the group consisting of an analyte, a prion, a protein, a polypeptide, a nucleic acid, a lipid, a carbohydrate, a biomolecule, a macromolecular complex, a fungus, and a microbial organism.
- 111. (New) The molecular biosensor of claim 109, wherein the target molecule is a protein or polypeptide.
 - 112. (New) The molecular biosensor of claim 109, wherein R¹ and R⁵ are each aptamers.
- 113. (New) The molecular biosensor of claim 109, wherein R¹ is a double stranded nucleic acid and R⁵ is an aptamer.

- 114. (New) The molecular biosensor of claim 109, wherein R¹ is an antibody and R⁵ is an aptamer.
- 115. (New) The molecular biosensor of claim 109, wherein R^1 is a double stranded nucleic acid and R^5 is an antibody.
- 116. (New) The molecular biosensor of claim 109, wherein R¹ and R⁵ are each antibodies.
- 117. (New) The molecular biosensor of claim 109, wherein R¹ and R⁵ are each double stranded nucleic acids.
- 118. (New) The molecular biosensor of claim 109, wherein R² and R⁶ comprise a nucleotide sequence having from about 10 to about 100 nucleotides in length.
- 119. (New) The molecular biosensor of claim 118, wherein R² forms a bond with each of R¹ and R³ and R⁶ forms a bond with each of R⁵ and R⁷, wherein the free energy of the formed bonds is from about 12.0 kcal/mole to about 16.5 kcal/ mole.
- 120. (New) The molecular biosensor of claim 119, wherein the bonds are covalent bonds.
- 121. (New) The molecular biosensor of claim 109, wherein R² and R⁶ are comprised of a bifunctional chemical crosslinker.
- 122. (New) The molecular biosensor of claim 109, wherein R² and R⁶ are from 0 to 500 angstroms in length.
- 123. (New) The molecular biosensor of claim 109, wherein R² and R⁶ are comprised of non-DNA polyethylene glycol and are from 0 to 500 angstroms in length.
 - 124. (New) The molecular biosensor of claim 109, wherein R³ and R⁷ are from about 4

to about 15 nucleotides in length.

- 125. (New) The molecular biosensor of claim 109, wherein the R⁴ and R⁸ comprise a pair of molecules that transfer energy thereby producing a detectable signal.
- 126. (New) The molecular biosensor of claim 109, wherein the detection means is selected from the group consisting of FRET, fluorescence cross-correlation spectroscopy, flourescence quenching, fluorescence polarization, flow cytometry, scintillation proximity, luminescense resonance energy transfer, direct quenching, ground-state complex formation, chemiluminescence energy transfer, bioluminescence resonance energy transfer, excimer formation, colorimetric substrates detection, phosphorescence, electro-chemical changes, and redox potential changes.
- 127. (New) A molecular biosensor, the biosensor having two nucleic acid constructs, the nucleic acid constructs comprising:

$$R^{1}-R^{2}-R^{3}-R^{4}$$
; and $R^{5}-R^{6}-R^{7}-R^{8}$:

wherein:

R¹ is an epitope binding agent that binds to a first epitope on a target molecule and is selected from the group consisting of an aptamer, an antibody, and double stranded nucleic acid;

 R^2 is a flexible linker attaching R^1 to R^3 by formation of a covalent bond with each of R^1 and R^3 , wherein R^2 comprises a bifunctional chemical crosslinker and is from 0 to 500 angstroms in length;

R³ and R⁷ are a pair of complementary nucleotide sequences from about 4 to about 15 nucleotides in length and having a free energy for association from about 5.5 kcal/mole to about 8.0 kcal/mole at a temperature from about 21° C to about 40° C and at a salt concentration from about 1 mM to about 100 mM;

R⁴ and R⁸ together comprise a detection means selected from the group consisting of FRET, fluorescence cross-correlation spectroscopy, flourescence quenching, fluorescence polarization, flow cytometry, scintillation proximity, luminescense resonance energy transfer, direct quenching, ground-state complex formation, chemiluminescence energy

transfer, bioluminescence resonance energy transfer, excimer formation, colorimetric substrates detection, phosphorescence, electro-chemical changes, and redox potential changes;

R⁵ is an epitope binding agent that binds to a second epitope on the target molecule and is selected from the group consisting of an aptamer, an antibody, and double stranded nucleic acid; and

R⁶ is a flexible linker attaching R⁵ to R⁷ by formation of a covalent bond with each of R⁵ and R⁷, wherein R⁶ comprises a bifunctional chemical crosslinker and is from 0 to 500 angstroms in length.

128. (New) A molecular biosensor, the biosensor having two aptamer constructs, the aptamer constructs comprising:

$$R^{1}-R^{2}-R^{3}-R^{4}$$
; and $R^{5}-R^{6}-R^{7}-R^{8}$;

wherein:

R¹ is an aptamer that binds to a first epitope on a target molecule;

 R^2 is a flexible linker attaching R^1 to R^3 ;

R³ and R⁷ are a pair of complementary nucleotide sequences having a free energy for association from about 5.5 kcal/mole to about 8.0 kcal/mole at a temperature from about 21° C to about 40° C and at a salt concentration from about 1 mM to about 100 mM; R⁴ and R⁸ together comprise a detection means such that when R³ and R⁷ associate a detectable signal is produced;

 R^5 is an aptamer that binds to a second epitope on the target molecule; and R^6 is a flexible linker attaching R^5 to R^7 .

129. (New) The molecular biosensor of claim 128, wherein the biosensor comprises:

$$R^{1}-R^{2}-R^{3}-R^{4}$$
; and $R^{5}-R^{6}-R^{7}-R^{8}$;

wherein:

R1 is an aptamer that binds to a first epitope on a target molecule;

R² is a flexible linker attaching R¹ to R³ by formation of a covalent bond with each of R¹ and R³, wherein R² comprises a bifunctional chemical crosslinker and is from 0 to 500 angstroms in length;

R³ and R⁷ are a pair of complementary nucleotide sequence from about 4 to about 15 nucleotides in length and having a free energy for association from about 5.5 kcal/mole to about 8.0 kcal/mole at a temperature from about 21° C to about 40° C and at a salt concentration from about 1 mM to about 100 mM;

R⁴ and R⁸ together comprise a detection means selected from the group consisting of FRET, fluorescence cross-correlation spectroscopy, flourescence quenching, fluorescence polarization, flow cytometry, scintillation proximity, luminescense resonance energy transfer, direct quenching, ground-state complex formation, chemiluminescence energy transfer, bioluminescence resonance energy transfer, excimer formation, colorimetric substrates detection, phosphorescence, electro-chemical changes, and redox potential changes;

R⁵ is an aptamer that binds to a second epitope on the target molecule; and R⁶ is a flexible linker attaching R⁵ to R⁷ by formation of a covalent bond with each of R⁵ and R⁷, wherein R⁶ comprises a bifunctional chemical crosslinker and is from 0 to 500 angstroms in length.

130. (New) A molecular biosensor having three nucleic acid constructs, the nucleic acid constructs comprising:

$$R^{15}$$
- R^{14} - R^{13} - R^{9} - R^{10} - R^{11} - R^{12} ;
 R^{16} - R^{17} - R^{18} - R^{19} ; and
 R^{20} - R^{21} - R^{22} - R^{23}

wherein:

 R^9 is an epitope binding agent that binds to a first epitope on a target molecule; R^{10} is a flexible linker attaching R^9 to R^{11} ;

R¹¹ and R²² are a first pair of complementary nucleotide sequences having a free energy for association from about 5.5 kcal/mole to about 8.0 kcal/mole at a temperature from about 21° C to about 40° C and at a salt concentration from about 1 mM to about 100 mM;

R¹² and R²³ together comprise a detection means such that when R¹¹ and R²² associate a detectable signal is produced;

R¹³ is a flexible linker attaching R⁹ to R¹⁴;

R¹⁴ and R¹⁸ are a second pair of complementary nucleotide sequences having a free energy for association from about 5.5 kcal/mole to about 8.0 kcal/mole at a temperature from about 21° C to about 40° C and at a salt concentration from about 1 mM to about 100 mM;

R¹⁵ and R¹⁹ together comprise a detection means such that when R¹⁴ and R¹⁸ associate a detectable signal is produced;

R¹⁶ is an epitope binding agent that binds to a second epitope on a target molecule;

 R^{17} is a flexible linker attaching R^{16} to R^{18} ;

 R^{20} is an epitope binding agent that binds to a third epitope on a target molecule; and R^{21} is a flexible linker attaching R^{20} to R^{22} .